

Application No. 10/522,252
Amendment dated August 31, 2006
First Preliminary Amendment

Docket No.: 022290.0123PTUS

AMENDMENTS TO THE CLAIMS

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1-15. (Canceled)

16. (New) Orally administered microcapsules for modified release of at least one active principle with low solubility,
wherein the mean diameter of the microcapsules are less than 1000 microns;
wherein each microcapsule has a core comprising at least one active principle and at least one solubilizing agent, wherein the at least one solubilizing agent is capable of increasing the solubility of the at least one active principle by more than 50% when the at least one solubilizing agent is placed in an aqueous solution at a concentration of 20% w/w at 37°C;
wherein the core is coated with a coating film which controls the modified release of the active principles;
wherein the coating film is at least 3% dry weight/dry weight of the microcapsule mass;
wherein the coating film of each microcapsule comprises at least one film-forming polymer (P1) insoluble in gastrointestinal tract fluids, at least one water-soluble polymer (P2), and at least one plasticizer, (PL).

17. (New) The microcapsules of claim 16,
wherein the mass fraction by dry weight of P1 relative to the total mass of the coating is between 40 and 90%;
wherein the mass fraction by dry weight of P2/P1+P2 is between 15 and 60% relative to the total mass of the coating; and
wherein the mass fraction by dry weight of PL/P1+PL is between 1 and 30% relative to the total mass of the coating.

18. (New) The microcapsules of claim 16, wherein the at least one solubilizing agent confers properties upon the core such that in a dissolving test (TD) a non-coated core releases 80% of the at least one active principle in less than two hours.

19. (New) The microcapsules of claim 16, wherein the at least one solubilizing agent is selected from the group consisting of hydrophilic polymers, polyvinyl pyrrolidone, polyvinyl alcohol, hydrophilic derivatives of cellulose, hydroxypropylcellulose, carboxymethylcellulose, maltodextrins, polyethylene glycol, surfactants, polyoxyethylene-polyoxypropylene copolymers, polyoxyethylenated hydrogenated castor oil, sodium dodecyl sulfate, esters of sucrose or sorbitan,

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phospholipids, polyethylene glycol stearate, disodium pamoate, polyoxyethylenated oils, polysorbates, sequestering agents, cyclodextrins, and mixtures thereof.

20. (New) The microcapsules of claim 16, wherein the mass fraction [solubilizing agent] x 100/[solubilizing agent + API] is greater than or equal to 5%.

21. (New) The microcapsules of claim 16, wherein P1 is selected from the group consisting of water-insoluble derivatives of cellulose, ethylcellulose, cellulose acetate, acrylic derivatives, poly(vinyl acetates), and mixtures thereof.

22. (New) The microcapsules of claim 16, wherein P2 is selected from the group consisting of water-soluble derivatives of cellulose, polyacrylamides, poly-N-vinylamides, poly (N-vinyl lactams), polyvinyl alcohols, polyoxyethylenes, polyvinylpyrrolidones, and mixtures thereof.

23. (New) The microcapsules of claim 16, wherein PL is selected from the group consisting of glycerol, glycerol esters, acetylated glycerides, glyceryl monostearate, glyceryl triacetate, glyceryl tributyrate, phthalates, dibutyl phthalate, diethyl phthalate, dimethyl phthalate, dioctyl phthalate, citrates, acetyl tributyl citrate, acetyl triethyl citrate, tributyl citrate, triethyl citrate, sebacates, diethyl sebacate, dibutyl sebacate, adipates, azelates, benzoates, plant oils, fumarates, diethyl fumarate, malates, diethyl malate, oxalates, diethyl oxalate, succinates, dibutyl succinate, butyrates, cetyl alcohol esters, malonates, diethyl malonate, castor oil and mixtures thereof.

24. (New) The microcapsules of claim 16, wherein the at least one active principle is selected from the group consisting of antiulcer agents, antidiabetic agents, anticoagulants, antithrombics, blood lipid-lowering agents, antiarrhythmics, vasodilators, antiangina agents, antihypertensives, vasoprotective agents, fertility promoters, inducers and inhibitors of uterine labor, contraceptives, antibiotics, antifungal agents, antiviral agents, anticancer agents, anti-inflammatories, analgesics, antiepileptics, antiparkinsonian agents, neuroleptics, hypnotics, anxiolytics, psychostimulants, antimigraine agents, antidepressives, antitussives, antihistamines, antiallergic agents, and mixtures thereof.

25. (New) The microcapsules of claim 24, wherein the at least one active principle is selected from the group consisting of prazosine, acyclovir, nifedipine, naproxen, ibuprofen, ketoprofen, fenoprofen, indomethacine, diclofenac, sulpiride, terfenadine, carbamazepine,

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fluoxetine, alprazolam, famotidine, ganciclovir, spironolactone, acetylsalicylic acid, quinidine, morphine, amoxicillin, paracetamol, metoclopramide, verapamil and mixtures thereof.

26. (New) The microcapsules of claim 16, wherein the coating film further comprises at least one lubricating surfactant (TA).

27. (New) The microcapsules of claim 26, wherein the TA is in a proportion of between 2 and 20% of the total mass of the dry coating.

28. (New) The microcapsules of claims 26, wherein the TA is selected from the group consisting of anionic surfactants, alkali metal salts, alkaline-earth metal salts of fatty acids, stearic acid, oleic acid, nonionic surfactants, polyoxyethylenated oils, polyoxyethylenated hydrogenated castor oil, polyoxyethylene-polyoxypropylene copolymers, polyoxyethylenated sorbitan esters, polyoxyethylenated castor oil derivatives, stearates, calcium stearate, magnesium stearate, aluminum stearate, zinc stearate, stearyl fumarates, sodium stearyl fumarate, glyceryl behenate, and mixtures thereof.

29. (New) A medicinal product comprising the microcapsules of claim 16.

30. (New) The medicinal product of claim 29, wherein the product is in a form selected from the group consisting of tablet, gelatin capsule, powder, and aqueous suspension.

31. (New) A medicinal product which comprises at least one active principle with low solubility, wherein the product is administered orally and released in vivo in a controlled, prolonged and, delayed manner,

wherein the medicinal product comprises microcapsules with a mean diameter of less than 1000 microns;

wherein each microcapsule has a core comprising at least one active principle and at least one solubilizing agent,

wherein the core is coated with a coating film comprising at least one film-forming polymer (P1) insoluble in gastrointestinal tract fluids, at least one water-soluble polymer (P2), and at least one plasticizer (PL),

wherein the coating film is at least 4% dry weight/dry weight of their total mass, and

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wherein the at least one solubilizing agent is one which when placed in an aqueous solution at a concentration of 20% w/w at 37°C increases the solubility of the active principle by more than 50%.